

Mixing large doses of both acetaminophen painkiller and caffeine may increase risk of liver damage

September 26 2007

Consuming large amounts of caffeine while taking acetaminophen, one of the most widely used painkillers in the United States, could potentially cause liver damage, according to a preliminary laboratory study reported in the Oct. 15 print issue of ACS' *Chemical Research in Toxicology*, a monthly journal.

The toxic interaction could occur not only from drinking caffeinated beverages while taking the painkiller but also from using large amounts of medications that intentionally combine caffeine and acetaminophen for the treatment of migraine headaches, menstrual discomfort and other conditions, the researchers say.

Health experts have warned for years that consuming excess alcohol while taking acetaminophen can trigger toxic interactions and cause liver damage and even death. However, this is the first time scientists have reported a potentially harmful interaction while taking the painkiller with caffeine, the researchers say.

While the studies are preliminary findings conducted in bacteria and laboratory animals, they suggest that consumers may want to limit caffeine intake -- including energy drinks and strong coffee -- while taking acetaminophen.

Chemist Sid Nelson, Ph.D., and colleagues, of the University of

Washington in Seattle, tested the effects of acetaminophen and caffeine on *E. coli* bacteria genetically engineered to express a key human enzyme in the liver that detoxifies many prescription and nonprescription drugs. The researchers found that caffeine triples the amount of a toxic byproduct, N-acetyl-p-benzoquinone imine (NAPQI), that the enzyme produces while breaking down acetaminophen. This same toxin is responsible for liver damage and failure in toxic alcohol-acetaminophen interactions, they say.

In previous studies, the same researchers showed that high doses of caffeine can increase the severity of liver damage in rats with acetaminophen-induced liver damage, thus supporting the current finding.

“People should be informed about this potentially harmful interaction,” Nelson says. “The bottom line is that you don’t have to stop taking acetaminophen or stop taking caffeine products, but you do need to monitor your intake more carefully when taking them together, especially if you drink alcohol.”

Nelson points out that the bacteria used in the study were exposed to ‘megadoses’ of both acetaminophen and caffeine, much higher than most individuals would normally consume on a daily basis. Most people would similarly need to consume unusually high levels of these compounds together to have a dangerous effect, but the toxic threshold has not yet been determined, he says.

Certain groups may be more vulnerable to the potentially toxic interaction than others, Nelson says. This includes people who take certain anti-epileptic medications, including carbamazepine and phenobarbital, and those who take St. John’s Wort, a popular herbal supplement. These products have been shown to boost levels of the enzyme that produces the toxic liver metabolite NAPQI, an effect that

will likely be heightened when taking both acetaminophen and caffeine together, he says.

Likewise, people who drink a lot of alcohol may be at increased risk for the toxic interaction, Nelson says. That's because alcohol can trigger the production of yet another liver enzyme that produces the liver toxin NAPQI. The risks are also higher for those who take large amounts of medications that combine both acetaminophen and caffeine, which are often used together as a remedy for migraine headaches, arthritis and other conditions.

The researchers are currently studying the mechanism by which this toxic interaction occurs and are considering human studies in the future, they say. The National Institutes of Health funded the initial animal and bacterial studies.

Source: American Chemical Society

Citation: Mixing large doses of both acetaminophen painkiller and caffeine may increase risk of liver damage (2007, September 26) retrieved 18 April 2024 from <https://phys.org/news/2007-09-large-doses-acetaminophen-painkiller-caffeine.html>

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